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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/780,600	02/09/2001	Joe Y.L. Lam	4446D1	9004

22896 7590 10/31/2002

PATTI SELAN, PATENT ADMINISTRATOR
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FOSTER CITY, CA 94404

EXAMINER

BAKER, MAURIE GARCIA

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 10/31/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

FILE

Office Action Summary

Application No.
09/780,600

Applicant(s)

Lam et al

Examiner
Maurie G. Bak r, Ph.D.

Art Unit
1639

-- The MAILING DATE of this communication appears on the cover sheet with the corresponding address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE THREE MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Aug 13, 2002

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 46-75 is/are pending in the application

4a) Of the above, claim(s) 66-75 is/are withdrawn from consideration

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 46-65 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirements.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. _____.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

4) ☐ Interview Summary (PTO-413) Paper No(s). _____

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

5) ☐ Notice of Informal Patent Application (PTO-152)

3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5

6) ☐ Other:

DETAILED ACTION

Please note: The number of Art Unit 1627 has been changed to 1639. Please direct all correspondence for this case to Art Unit **1639**.

1. The Response filed via facsimile on August 13, 2002 (Paper No. 4) is acknowledged. No claims were cancelled, added or amended in this response. Therefore, claims 46-75 are pending.

Election/Restriction

2. Applicant's election of Group I (claims 46-65) and election of species is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 66-75 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions. Election was made without traverse in Paper No. 4 (see above).

4. With respect to the species election, the elected species was searched and not found in the prior art. Thus, the search was extended as per MPEP § 803.02 (cited below):

On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the

Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration.

5. No prior art was found that anticipates or renders obvious the instant claims, therefore the species election requirement is withdrawn and claims 46-65 are examined on the merits in this action.

Information Disclosure Statement

6. The information disclosure statement filed 2/09/01 fails to fully comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent, publication, or other information listed that is not in the English language. It has been placed in the application file, but the information referred to therein with respect to the foreign patents DD 223149 & EP 0543333 and articles by Kamel et al & Zander et al have not been considered. These documents are not in the English language and no English Abstract or any other documentation was provided.

Claim Objections

7. Claims 62 and 65 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claims appear

to broaden the scope of claim 46 (on which they depend). This is because they appear to be drawn to dyes outside the scope of claim 46. See also rejections under 35 USC 112, first and second paragraphs below.

8. Also, claim 55 is objected to because the claim does not end with a period. This is improper and correction is requested.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 57, 62, 64 and 65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The specification as originally filed fails to support the invention as now claimed. First, claims 57 and 64 are drawn to specific species of compounds that do not appear to be supported. Note that a generic disclosure is **not** sufficient support for a specific entity within the class. Second, there does not appear to be support for compounds having “D is a donor dye and an acceptor dye” or “where

NUC is a polynucleotide labeled with a donor dye and an acceptor dye” as recited in instant claims 62 and 65, respectively. In accordance with MPEP § 714.02, applicants **should specifically point out support** for any amendments.

11. Claims 46-65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. Applicant’s claims are directed to a “labeled nucleic acid compound” that comprises a moiety denoted L that is defined only as “a linkage”. This term could encompass an enormous variety of different entities. It is noted that some of the instant claims (i.e. claims 59 and 60) do appear to define the linkage; however, the scope of these claims is unclear and thus they are included in this rejection. See rejection under 35 USC 112, second paragraph below.

The language of the specification should describe the claimed invention so that one skilled in the art can recognize what is claimed. A description of a compound in terms of its function fails to distinguish the compound from others having the same activity or function. A description of what a material does, rather

than of what it is, usually does not suffice. The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175).

The specification discloses only limited examples of the preparation and use of such “linkage[s]”. This portion of the molecule could encompass very different moieties such as various inorganic and organic entities of varying structure. Applicant’s claimed scope represents only an invitation to experiment regarding possible “linkage[s]”. The disclosure is neither representative of the claimed genus, nor does it represent a substantial portion of the claimed genus. Moreover, the claimed genus encompasses members which are yet to be prepared or envisioned. This further evidences that instant disclosure does not constitute support for the claimed genus or a substantial portion thereof.

12. Claims 62 and 65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy

the enablement requirement and whether any necessary experimentation is

“undue”. These factors include, but are not limited to:

- (1) the breadth of the claims;
- (2) the nature of the invention;
- (3) the state of the prior art;
- (4) the level of one of ordinary skill;
- (5) the level of predictability in the art;
- (6) the amount of direction provided by the inventor;
- (7) the existence of working examples; and
- (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The breadth of the claims and the nature of the invention: Claim 62 is drawn to a compound where “D is a donor dye and an acceptor dye” and claim 65 is drawn to a compounds “where NUC is a polynucleotide labeled with a donor dye and an acceptor dye”. The claims go on to recite that fluorescence energy transfer occurs. The invention is such that each of the components must be present in operable form for successful practice of the invention. That is, one must be able to make and use each of the portions of the instant compounds. The state of the prior art and the level of predictability in the art: While various fluorescence energy transfer systems were known in the art at the time of filing, the specification gives no guidance to permit one of skill in the art to devise strategies for making and using any compound having “D is a donor dye and an acceptor dye” or “where NUC is a polynucleotide labeled with a donor dye and an acceptor dye”. The structures of possible variants are sufficiently diverse as to require further research as to how to make and use such compounds. Moreover, one of ordinary skill would not know, *a priori*, how such a system should be configured

(i.e. structure, linkage) from the components set forth in the instant claim. The level of one of ordinary skill: The level of skill would be high, most likely at the Ph.D. level. Such persons of ordinary skill in this art, given its unpredictability, would have to engage in undue (non-routine) experimentation to carry out the invention as claimed. The amount of direction provided by the inventor and the existence of working examples: Applicants have not provided *any* examples of compounds having “D is a donor dye and an acceptor dye” or “where NUC is a polynucleotide labeled with a donor dye and an acceptor dye”. Thus, further research would be necessary to make or use such a system as the practice of such would not be predictable. The quantity of experimentation needed to make or use the invention based on the content of the disclosure: The instant specification does not provide to one skilled in the art a reasonable amount of guidance with respect to the direction in which the experimentation should proceed in making and using the claimed compounds. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 & n.23 (Fed. Cir. 1991). Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed.

13. Claims 46-65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds comprising *defined linkage sites on*

the D moiety and a *structurally defined linkage (L)*, does not reasonably provide enablement for compounds containing **any** linkage group linked at any site of D. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

It is clear from applicant's specification how one might practice this invention with *defined linkage sites on the D moiety* and *defined linkers*; however, there is insufficient guidance as to how to make/use compounds comprising **any** linkage group linked at any site of D. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include, but are not limited to:

- (1) the breadth of the claims;
- (2) the nature of the invention;
- (3) the state of the prior art;
- (4) the level of one of ordinary skill;
- (5) the level of predictability in the art;
- (6) the amount of direction provided by the inventor;
- (7) the existence of working examples; and
- (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The breadth of the claims and the nature of the invention: The claims are drawn to compounds comprising NUC, L and D portions that are linked together. In claims 46-58, 62, 63 and 65 no limitations on the identity of L are given (defined only as "a linkage") and, as such, this could read on a wide variety of structures. Such represents very broad scope. It is noted that claims 59-61 and 64 appear to recite

specific L groups and/or linkage sites on D. However, the linkage sites and the structure of the linker for these compounds is not set forth clearly (see rejections under 35 USC 112, second paragraph below), and for none of the claims are *both* defined. This also represents broad scope. The state of the prior art and the level of predictability in the art: Labeled nucleic acid compounds were known in the art at the time of filing; however, only limited numbers of such compounds were known and the specification gives no guidance to permit one of skill in the art to devise strategies for synthesis of *any* nucleic acid compound that has a dye linked thereto in any manner with any linkage group. The structures of possible variants are sufficiently diverse and one of ordinary skill would not be able to predict their structures. The limitation that the NUC, L and D portions are linked together adds to the unpredictability because the portions have various structures each of which would require completely different linkage strategies. One of ordinary skill could not guess, *a priori*, how to make and use **any** such compounds as one could not necessarily predict the linkage site and linkage structure in the absence of any guidance without undue experimentation. Applicant's claimed scope of compounds represents only an invitation to experiment regarding possible compounds with undefined linkage sites linked with linkers of undefined structure. The level of one of ordinary skill: The level of skill would be high, most likely at the Ph.D. level. Such persons of ordinary skill in this art, given its unpredictability, would have to engage in undue (non-routine) experimentation to carry out the invention as claimed. The amount of direction provided by the

inventor and the existence of working examples: Applicants have only provided very limited examples of compounds within the scope of the claims. These examples only show the NUC and D portions linked together in a *defined* manner, with a *defined* L group. No generic strategy for determining linkage sites on the D moiety is provided. The teachings of the instant specification coupled with the examples only supports specific labeled nucleic acid compounds that are linked at *a defined linkage site of D with a defined linkage group (L)*. The quantity of experimentation needed to make or use the invention based on the content of the disclosure: The instant specification does not provide to one skilled in the art a reasonable amount of guidance with respect to the direction in which the experimentation should proceed in making and using the full scope of the claimed compounds. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 & n.23 (Fed. Cir. 1991). Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure, one of ordinary skill would not have a reasonable expectation of success and the practice of the full scope of the invention would require undue experimentation.

Claim Rejections - 35 USC § 112

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 46, 50, 53, 55, 59, 60, 62 and 65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 46 recites confusing Markush language for the definition of D.

There is no conjunction between the structures whatsoever. It is suggested to use standard Markush language; see MPEP 2173.05(h) concerning alternative expressions:

Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. One acceptable form of alternative expression, which is commonly referred to as a Markush group, recites members as being "selected from the group consisting of A, B and C." See *Ex parte Markush*, 1925 C.D. 126 (Comm'r Pat. 1925). When materials recited in a claim are so related as to constitute a proper Markush group, they may be recited in the conventional manner, or alternatively. For example, if "wherein R is a material selected from the group consisting of A, B, C and D" is a proper limitation, then "wherein R is A, B, C or D" shall also be considered proper.

B. Claim 46 also recites "analog thereof" in the Markush group for NUC. It is unclear what would or would not comprise an "analog" as claimed. The specification does not provide a standard for ascertaining such terms, and thus one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

C. Claims 50 and 53 include in the definitions of R₈ a "linkage" (claim 50) or an L moiety defined as "a linkage" (claim 53). These claims are completely confusing as it is unclear if the "linkage" or L defined in these

dependent claims is the same or different from the L set forth in independent claim 46.

- D. Claim 55 recites “phosphate analog” in the Markush group for W₃. It is unclear what would or would not comprise an “phosphate analog” as claimed. The specification does not provide a standard for ascertaining such terms, and thus one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.
- E. Claims 59 and 60 recite “wherein L is attached to a nucleobase of NUC and to D in the structure: ...”. This language is deemed to be confusing. It is unclear whether the structure between the NUC and the D groups in the structures shown in the claim is supposed to be the L moiety. Language such as ---wherein L is attached to a nucleobase of NUC and to **D to form** the structure: --- is suggested.
- F. Claims 62 and 65 recite “D is a donor dye and an acceptor dye” and “where NUC is a polynucleotide labeled with a donor dye and an acceptor dye”, respectively. The recitation of “donor dye and an acceptor dye” is completely confusing and lacks antecedent basis, as there is only one dye (D) in claim 46 (from which claims 62 and 65 depend). Thus, the claims are deemed to be indefinite as it is unclear as to applicant’s intent.

Status of Claims/Conclusion

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maurie Garcia Baker, Ph.D. whose telephone number is (703) 308-0065. The examiner can normally be reached on Monday-Thursday and alternate Fridays from 9:30 to 7:00.

18. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang, can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Maurie Garcia Baker, Ph.D.
October 29, 2002

A handwritten signature in black ink, consisting of stylized, overlapping loops and a long horizontal stroke extending to the right.

MAURIE GARCIA BAKER, Ph.D.
PATENT EXAMINER